UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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APR 28 1993

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Registration of Castor Oil (Technical Grade): SAB Review of Product Characterization Data and Toxicity Studies (DP Barcode No.: D185680; Submission No.: S430158; I.D. No.: 064439-R Mole Med; MRID No.: 425489-00. -02 through -07)

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JTMc 4/26/93

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BACKGROUND INFORMATION: On Wednesday, February 17, 1993, representatives of the Ad Hoc Screening Committee for Reduced Risk Pesticides convened and determined that castor oil should be a candidate for the reduced data requirements. The committee agreed that castor oil satisfied the necessary criteria as set forth in the Guidance document; and, therefore, is subject to a reduced data set (see 09 March 1993 memorandum from Ad Hoc Committee to OPP Division Directors). Consequently no further toxicology data, as set forth in Part 158, are necessary or appropriate in order to complete the assessment on the pesticidal active ingredient as required under FIFRA for the purpose of registration.

The registrant has submitted several acute toxicity studies which have been reviewed by the Science Analysis Branch (SAB). Attached are the product characterization and mammalian toxicology study summaries for castor oil (technical grade material), a biochemical pesticide proposed for use to repel moles. It should be noted that although certain studies were classified as supplementary the registrant is NOT required to repeat these studies based on the rationale provided previously (see 09 March 1993 memorandum).

ACTION REQUESTED: Mole Med, Inc. has submitted product characterization data and a battery of acute mammalian toxicology

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studies to support the registration of castor oil (technical grade material). SAB has summarized the study results below.

CONCLUSION: The registrant should submit the details of the manufacturing process which leads to the production of U.S. Pharmacopeia (USP) grade castor oil, unless the registrant only purchases castor oil certified as USP grade. In the later instance, the registrant should submit the source(s) and label certifying USP grade oil. If certified USP grade castor oil is not used then the Agency will assume that this is a new technical grade material for which all toxicology and product identity/chemistry data may be required.

The lack of significant toxicity in the acute mammalian toxicity studies, and the lack of toxicity in the human dermal sensitization study support the conclusion by the Ad Hoc committee that the mammalian toxicology data waivers were appropriate.

STUDY SUMMARIES:

Product Identity/Chemistry

Adequate information and data were submitted to fulfill the requirements of Subdivision M Series 151A-10 through -17 for the technical grade material, castor oil, provided that USP grade oil is used. SAB has noted some deficiencies and has requested data and/or additional information which is specified below.

151A-10. Product Identity. Castor oil, a natural product derived the castor bean, is a mixture of triglycerides (ricinoleic, oleic, linoleic, palmitic and stearic acids). The registrant states that the active ingredient, castor oil (CAS #8001-79-4), will be USP grade (FDA approved) material. Information on the source and a description of beginning materials, other than castor bean, have not been provided, and are not needed provided that the manufacturing process produces a USP grade oil.

151A-11. Manufacturing Process. A brief summary of the manufacturing process was provided. Castor oil is extracted from the castor plant by pressing the seeds, then refined by a caustic procedure to produce USP grade oil. A step-by-step detailed description of the manufacturing process used to produce the technical grade material must be provided to the Agency unless the registrant only purchases USP grade castor oil.

151A-13. Analysis of Samples. Castor oil, consisting primarily of ricinoleic acid, may contain trace levels of sodium soaps of the fatty acids as well as 9,11- and 9,12-linoleic acid. A detailed description of the procedures and/or methodologies used to identify any unintentional ingredients at levels greater than or equal to 1% must be submitted unless USP grade oil is used.

151A-15. Certification of Ingredient Limits. A CSF for the technical grade material must be submitted. The registrant states

that castor oil "...is about 90% to 87% triglycerides of ricinoleic acid..." and the "...amount can vary as much as 5% depending on location, time and manufacturer." No other information was submitted. Since the content of castor oil will vary from batch to batch, SAB presumes that the batches will be blended to achieve the concentration as stated on the label. This information should be submitted to the Agency. As long as the manufacturing process produces USP grade oil, the technical grade material would comprise approximately 100% of the active ingredient. If appropriate, certified limits for impurities at levels greater than or equal to 1% must be submitted.

151A-16. Analytical Methods for Certified Limits. The submission did not provide any information on the techniques and/or methodologies used for the analysis of the active ingredient. Instead "typical values" were provided by the registrant. Such "values" included the typical acid value of 2, a typical value of 86 for the "iodine value," the typical saponification number of 180, and the hydroxyl number or value of 164. A description of the analytical methods used to determine the amount of castor oil in the technical product was not provided and assuming that these parameters are used to ascertain a USP grade product, are not required unless the manufacturing process changes.

151A-17. Physical and Chemical Properties. Adequate information was submitted to fulfill the requirements of Series 151A-17. The following information was submitted for the technical material:

Color	Colorless to pale yellow
Physical State	Liquid (oil)
Odor	Slightly acid w/ aftertaste
Boiling Range	312°C (595°F)
Density g/ml @ 15°C	0.961-0.963
Solubility	Soluble in ether, 95% ethanol, methanol, glacial acetic acid Insoluble in water
Vapor Pressure	Log KPa Est. -4 to -6
Part. Coefff.	Log Coef 5 to 8
pH	5-7
Viscosity	7.3 Stokes @ 25°C
Flash Point	555°F
Auto Ignition Temp.	840°F
Corrosive Charact.	Non-corrosive

Mammalian Toxicology
Technical Grade of the Active Ingredient

The toxicology studies were performed with the technical grade material (i.e. USP grade castor oil). These studies were evaluated but not given a "full review" because the active ingredient met the criteria set forth in the Reduced Data Requirement Guidance document (see 09 March 1993 memorandum). Consequently, all

toxicology data requirements for USP grade castor oil have been waived.

425489-03

151B-10 - Acute Oral Toxicity Study in Rats. Following the administration of a single oral dose (5 gm/kg of body weight) of USP grade castor oil, the LD_{50} was determined to be greater than 5 gm/kg. No mortality was noted in any of the treated animals (5 males and 5 females) throughout the course of the 14 day study.

Discussion: This study would be classified as supplementary because the following data and/or information was not provided: a) the composition of the test material, b) individual animal data, c) body weight, d) clinical signs or observations, and results or findings upon necropsy. However, this study does not need to be repeated based on the 03/09/93 memorandum waiving this requirement for USP grade oil.

151B-11. Acute Dermal Toxicity Study. The registrant has requested a waiver for this study provided that the technical grade material is USP grade castor oil. Although no rationale was provided SAB would support this request and would not require this study be performed as long as USP grade oil is used. In addition, experience has shown that through long historical use, this material is not, nor expected to be toxic from dermal application.

151B-12. Acute Inhalation Toxicity Study. This study was not preformed and is not needed based on the rationale provided in the reduced data waiver set (see 151B-11 above and 03/09/93 memorandum).

425489-04

151B-13. Primary Eye Irritation Study in Rabbit. Following instillation of the technical grade material (amount not specified), conjunctival effects (i.e. redness) were observed in 4 of 6 rabbits at 24 hr. These effects were resolved during the 72 hr observation period. No corneal involvement was observed. No other data or information was provided.

Discussion: This study would be classified as supplementary because the following data and/or information was not provided: a) the composition of the test material, b) individual animal data, c) instillation procedure(s), d) amount of test material delivered, and e) if the treated eye(s) was washed after instillation of the test material. This test does not need to be repeated since USP grade oil was used as the test material and since an eye irritation study on the end use product will provide information for labeling statement (refer to rationale provided in 151B-10).

425489-05

151B-14. Primary Dermal Irritation Study in Rabbits. When applied to the shaved backs of six rabbits (for 24 hr) a single dose (0.5 gm or 0.5 ml) of the test material (USP grade castor oil) caused minimal erythema in one animal (intact and abraded), and in the abraded skin of two additional animals, with both conditions present at 72 hr post-treatment. Edema was observed in the abraded skin of one of six animals at 72 hr post-treatment. Based on these

results the test material was not considered a primary skin irritant.

42548906

151B-15. Dermal Sensitization. A study was performed on 106 human volunteers whereby Castor Oil Crystal O was applied to the skin for 48 hr. The amount of test material was not provided. The test material elicited a reaction in one person at 48 hr post-treatment (2 out of 4) which was reduced by 72 hr (1 out of 4). The study indicated that under the conditions used in this study the test material was not considered a dermal sensitizer.

151B-16. Hypersensitivity Incidents. Although incidents are not anticipated, the registrant is required to report any such occurrences to the Agency.

151B-17. Mutagenicity. This study requirement was not addressed by the registrant. If USP grade oil is used SAB would not recommend that these studies be performed (see 03/09/93 memorandum).